108. A pharmaceutical composition comprising a carrier; a nucleic acid in the form f an aerosol that comprises one or more oligonucleotide(s) (oligo(s)) effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, bronchoconstriction, allergy(ies) and/or inflammation, and contains up to and including about 15% adenosine (A), the oligo being anti-sense to an initiation codon, a coding region or a 5' or 3' intron-exon junctions of a gene encoding an adenosine A1, A2a, A2b or A3 receptor or anti-sense to their respective mRNA; pharmaceutically and veterinarily acceptable salts of the oligo(s) or mixtures thereof; and a surfactant that may be operatively linked to the nucleic acid.

109. The composition of claim 108, wherein the oligo consists of up to about 10% A.

110. The composition of claim 109, wherein the oligo consists of up to about 5% A.

111. The composition of claim 110, wherein the oligo consists of up to about 3% A.

112. The composition of claim 111, wherein the oligo is A-free.

113. The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3' intron-exon junctions or to sequences of the coding region comprising 2 or more G and/or C of the adenosine A1 receptor gene.

114. The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3' intron-exon junctions or to sequences of the coding region comprising 2 or more G and/or C of the adenosine A_{2a}, A_{2b} and/or A_3 receptors.

115. The composition of claim 108, wherein if the oligo contains adenosine (A), at least one A is substituted by a universal base selected from heteroaromatic bases which bind to a thymidine base but have antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} or A_3 receptors, or heteroaromatic bases that have no activity or have agonist activity at the adenosine A_{2a} receptor.

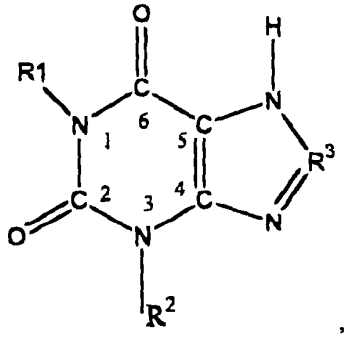
116. The composition of claim 115, wherein substantially all As are substituted by a universal base (s) selected from heteroaromatic bases that bind to a thymidine base but either have antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} or A_3 receptors, or heteroaromatic bases that have no activity or have agonist activity at the adenosine A_{2a} receptor.

117. The composition of claim 115, wherein the heteroaromatic bases are selected from pyrimidines or purines that may be substituted by O, halo, NH_2, SH, SO, SO_2, SO_3, COOH, or branched or fused primary or secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl,

arylalkynyl, or arylcycloalkyl, all of which may be further substituted by O, halo, NH_2, primary, secondary or tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl.

118. The composition of claim 117, wherein the pyrimidines are substituted at a 1, 2, 3, and/or 4 position, and the purines are substituted at a 1, 2, 3, 4, 7 and/or 8 position.

119. The composition of claim 118, wherein the pyrimidines or purines are selected from theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xantine having the chemical formula



wherein R^1 and R^2 are independently H, alkyl, alkenyl or alkynyl and R^3 is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl, NH_2-alkylamino-ketoxyalkyloxy-aryl or mono or dialkylaminoalkyl-N-alkylamino-SO_2 aryl.

120. The composition of claim 116, wherein the universal base is selected from 3 – nitropyrrole - 2' - deoxynucleoside, 5 –nitroindole, 2 - deoxyribosyl - (5- nitroindole), 2 – deoxyribofuranosyl - (5 - nitroindole), 2' - deoxyinosine, 2' - deoxynebularine, 6H, 8H - 3, 4 - dihydropyrimido [4, 5 - c] oxazine – 7 - one or 2 – amino – 6 - methoxyaminopurine.

121. The composition of claim 108, wherein a methylated cytosine (^mC) is substituted for an unmethylated cytosine (C) in at least one CpG dinucleotide if present in the nucleic acid(s).

122. The composition of claim 108, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-

iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

123. The composition of claim 122, wherein substantially all mononucleotides are linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

124. The composition of claim 108, wherein the oligo comprises about 7 to about 60 mononucleotides.

125. The composition of claim 108, wherein the oligo comprises SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA Sulfate), dehydroepiandrosterone sulfatide (DHEA

Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

126. The composition of claim 108, wherein the nucleic acid is linked to an agent that enhances cell internalization or up-take and/or a cell targeting agent.

127. The composition of claim 126, wherein the cell internalization or up take enhancing agent is a transferrin, a asialoglycoprotein or a streptavidin.

128. The composition of claim 126, wherein the cell targeting agent comprises a vector, and the nucleic acid is operatively linked to the vector.

129. The composition of claim 128, wherein the vector comprises a prokaryotic or eukaryotic vector.

130. The composition of claim 108, wherein the surfactant is selected from surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein D or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycero-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters, phosphatidyl ethers, palmitates, alcohols, tyloxapol, phospholipids, fatty acids, surfactant-associated proteins or $C_{22}H_{19}C_{10}$.

131. The composition of claim 130, wherein the surfactant is selected from polyoxy ethylene 23 lauryl ether (Brij 35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC®), tyloxapol (Exosurf®), phospholipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}C_{10}$ (Atovaquone®).

133. The composition of claim 108, wherein the carrier comprises a biologically acceptable carrier.

134. The composition of claim 108, wherein the carrier is a pharmaceutically or veterinarily acceptable carrier.

135. The composition of claim 134, wherein the carrier comprises gaseous, liquid or solid carriers.

136. The composition of claim 108, further comprising an agent selected from therapeutic agents other than the nucleic acid(s), antioxidants, flavoring or coloring agents, fillers, volatile oils, buffering agents, dispersants, RNA inactivating agents, flavoring agents, propellants or preservatives.

137. The composition of claim 136, comprising a pharmaceutically or veterinarily acceptable carrier, the nucleic acid, a surfactant, and other therapeutic agents.

138. The composition of claim 136, wherein the RNA inactivating agent comprises an enzyme.

139. The composition of claim 138, wherein the enzyme comprises a ribozyme.

140 The composition of claim 108, further comprising a propellant.

141. The composition of claim 108, wherein the nucleic acid is present in an amount of about 0.01 to about 99.99 w/w of the composition.

143. The formulation of claim 108, selected from intrabuccal, intrapulmonary, respirable, nasal, inhalable, intracavitary, intraorgan, or slow release formulations.

144. The formulation of claim 143, wherein the carrier is selected from a gaseous, solid or liquid carrier.

146. The aerosol or spray formulation of claim 108, which is selected from powders, sprays, solutions, suspensions or emulsions.

148. The aerosol or spray formulation of claim 108, which is selected from an aqueous or alcoholic solutions or suspensions, oily solutions or suspensions, or oil-in-water or water-in-oil emulsions.

151. A capsule or cartridge, comprising the formulation of claim 143.

152. The spray or aerosol formulation of claim 146, comprising a solid powdered spray or aerosol.

153. The formulation of claim 108, wherein the carrier comprises a hydrophobic carrier.

154. The formulation of claim 153, wherein the carrier comprises lipid vesicles and/or particles.

155. The formulation of claim 154, wherein the vesicles comprise liposomes, and the particles comprise microcrystals.

156. The formulation of claim 155, wherein the vesicles comprise liposomes that comprise the nucleic acid.

158. The formulation of claim 143, which comprises an intrapulmonary, intracavitary

or intraorgan liquid or solid powdered formulation of particle size about 0.5μ to about 10 μ, or about 10 μ to about 500 μ.

159. The formulation of claim 143, which comprises a nasal formulation of particle size about 10 μ to about 500 μ.

161. The formulation of claim 143, in bulk, or in single or multiple unit dose form.

162. The formulation of claim 143, which is a respirable or inhalable formulation of a solid powdered or liquid aerosol or spray of particle size about 0.5 μ to about 10 μ.

163. A single cell, comprising the nucleic acid of claim 108.

164. A kit for diagnosis or treatment of diseases and conditions associated with hypersensitivity to and/or increased levels of, adenosine and/or bronchoconstriction and/or lung allergy(ies) and/or inflammation and/or asthma comprising, in separate containers,

the delivery device of claim 222;

a nucleic acid comprising at least one oligonucleotide (oligo) effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, or to alleviate bronchoconstriction, asthma or lung allergy(ies) and/or inflammation, the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine, with bronchoconstriction, asthma, or lung allergy(ies) or inflammation, or being anti-sense to the corresponding mRNA; the nucleic acid comprising one or more oligo(s), their mixtures or their pharmaceutically or veterinarily acceptable salts; and

instructions for preparation of a respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation of particle size about 0.5 to about 500 μ and for its use; and

optionally an agent selected from therapeutic or diagnostic agents other than the oligo, anti-oxidants, fillers, volatile oils, dispersants, anti-oxidants, flavoring agents, propellants, preservatives, solvents, buffering agents, RNA inactivating agents, agents that are internalized or up-taken by a cell, or coloring agents.

165. The kit of claim 164, wherein the delivery device comprises a nebulizer that delivers single metered doses of a solid powdered or liquid aerosol or spray formulation of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ of the nucleic acid.

166. The kit of claim 164, wherein the device comprises an insufflator adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray; and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as a nasal, inhalable, respirable, intrapulmonary, intracavitary or

intraorgan formulation of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ.

167. The kit of claim 164, wherein the delivery device comprises a pressurized inhaler that delivers a solid powdered or liquid aerosol or spray of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ; and the nucleic acid is provided as a suspension, solution, emulsion or dry powder aerosol or spray formulation of about 0.5 μ to about 10 μ or about 10 μ to about 500 μ.

168. The kit of claim 164, comprising the delivery device, a surfactant, the nucleic acid and other therapeutic agents.

169. The kit of claim 164, wherein the solvent is selected from organic solvents or organic solvents mixed with one or more co-solvents.

170. The kit of claim 164, wherein the device is adapted for receiving a capsule(s) or cartridge(s), and the nucleic acid is separately provided as an inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation in a capsule(s) or cartridge(s).

171. The kit of claim 164 further comprising, in separate containes, a propellant, and pressurized means for delivery adapted for delivering a solid powdered or liquid aerosol or spray, and instructions for loading into the delivery device an inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation of the nucleic acid of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ, and then joining the device with the propellant and the pressurized means.

172. The kit of claim 167, wherein the pressurized inhaler further comprises a propellant and means for delivery of the propellant, and delivers the nucleic acid as a liquid or solid powdered aerosol or spray formulation.

173. An in vivo method of delivering a pharmaceutical composition to a target polynucleotide, comprising administering to the airways of a subject an aerosol or spray composition of particle size about 0.5 μ to about 500 μ comprising a nucleic acid which comprises at least one oligonucleotide (oligo) effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, or to alleviate bronchoconstriction, asthma and/or lung allergy(ies) and/or inflammation, the oligo containing up to and including about 15% adenosine (A), and being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine, bronchoconstriction, asthma, and/or lung allergy(ies) and/or inflammation, or being anti-sense to the corresponding mRNA; the nucleic acid comprising one or more oligo(s), pharmaceutically or veterinarily acceptable salts of the oligo(s), or mixtures of the oligo(s) or their salts.

178. The method of claim 173, wherein the composition is administered intrapulmonarily, intraorgan, intracavitarily, intrabuccally, intranasally, by inhalation or into the subject's respiratory system.

179. The method of claim 173, wherein the oligo is effective to reduce hyper-responsiveness to adenosine, the amount of the adenosine receptor or the production or availability of adenosine, or to increase the degradation of the adenosine receptor mRNA.

180. The method of claim 178, wherein the oligo is administered directly into the subject's lung (s), intraorgan, intracavitarily, intrabuccal or intrapulmonarily.

181. The method of claim 178, wherein the composition is administered as solid powdered or liquid particles of the nucleic acid about 0.5 to about 10 μ in size.

184. The method of claim 173, wherein the composition further comprises a surfactant.

185. The method of claim 173, wherein the hyper-responsiveness to, and/or increased levels of, adenosine, asthma or lung allergy(ies) or inflammation is associated with bronchoconstriction of lung airways.

186. The method of claim 185, wherein the hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, asthma or lung allergy(ies) or inflammation is associated with COPD, asthma, ARDS, RDS, CF or side effects of adenosine administration.

187. The method of claim 173, wherein the hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, asthma, or lung allergy(ies) or inflammation is associated with inflammation or an inflammatory disease.

188. The method of claim 173, wherein the composition further comprises other therapeutic agents.

189. The method of claim 188, wherein the therapeutic agent comprises anti-adenosine A_1, A_{2b} or A_3 receptor agents or adenosine A_{2a} receptor stimulating agents other than the nucleic acid(s).

191. The method of claim 184, wherein the surfactant comprises surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycero-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP

choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters, phosphatidyl ethers, palmitates, alcohols and tyloxapol, phospholipids, fatty acids, surfactant-associated proteins, or $C_{22}H_{19}C_{10}$.

192. The method of claim 173, wherein the subject is a mammal.

193. The method of claim 192, wherein the mammal is a human or a non-human mammal.

195. The method of claim 173, wherein the nucleic acid is administered in amount of about 0.005 to about 150 mg/kg body weight.

196. The method of claim 195, wherein the nucleic acid is administered in an amount of about 0.01 to about 75 mg/kg body weight.

197. The method of claim 196, wherein the nucleic acid is administered in an amount of about 1 to about 50 mg/kg body weight.

198. The method of claim 173, which is a prophylactic or therapeutic method.

200. The method of claim 173, wherein the nucleic acid is obtained by

(a) selecting fragments of a target nucleic acid having at least 4 contiguous bases consisting of G or C; and

(b) obtaining a second oligo 4 to 60 nucleotides long comprising a sequence that is anti-sense to the selected fragment, the second oligo having an A base content of up to and including about 15%.

201. The method of claim 173, wherein the oligo consists of up to about 10% A.

202. The method of claim 201, wherein the oligo consists of up to about 5% A.

203. The method of claim 201, wherein the oligo consists of up to about 3% A.

204. The method of claim 203, wherein the oligo is A-free.

205. The method of claim 173, wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding an adenosine A1, A2b or A3 receptor, and the composition further comprises a surfactant.

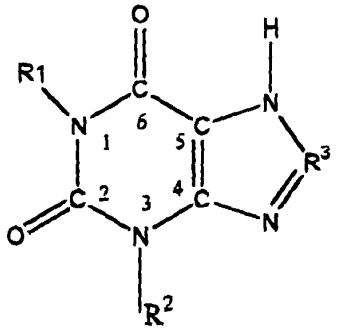
206. The method of claim 173, wherein if the oligo contains A, at least one A is substituted with a universal base selected from heteroaromatic bases which bind to a thymidine base but have antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} or A_3 receptors, or heteroaromatic bases which have no activity or have agonist activity at the adenosine A_{2a} receptor.

207. The method of claim 206, wherein substantially all As are substituted with universal bases selected from heteroaromatic bases which bind to a thymidine base but have antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} or A_3 receptors, heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a} receptor.

208. The method of claim 206, wherein the heteroaromatic bases are selected from pyrimidines or purines, that may be substituted by O, halo, NH_2, SH, SO, SO_2, SO_3, COOH branched fused primary secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, arylcycloalkyl, all of which may be further substituted by O, halo, NH_2, primary, secondary and tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl.

209. The method of claim 208, wherein the pyrimidines are substituted at positions 1, 2, 3 and\or 4, and the purines are substituted at positions 1, 2, 3, 4, 7 and\or 8.

210. The method of claim 209, wherein the pyrimidines and purines are selected from theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xantine having the chemical formula



wherein R^1 and R^2 are independently H, alkyl, alkenyl or alkynyl, and R^3 is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl, NH_2-alkylamino-ketoxyalkyloxy-aryl or mono or dialkylaminoalkyl-N-alkylamino-SO_2 aryl.

211. The method of claim 206, wherein the universal base comprises 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5-nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido [4,5-c] oxazine-7-one or 2-amino-6-methoxyaminopurine.

212. The method of claim 173, further comprising methylating at least one cytosine vicinal to a guanosine into a methylated cytosine (^{m}C) if a CpG dinucleotide is present in the oligo(s).

213. The method of claim 173, further comprising modifying or substituting at least one mononucleotide of the anti-sense oligo(s) with methylphosphonate, phosphotriester, phosphorothioate, phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene(methyimino), methyleneoxy (methylimino), 2'-O-methyl, phosphoramidate residues, or combinations thereof.

214. The method of claim 213, wherein substantially all mononucleotides are substituted and/or modified.

215. The method of claim 173, further comprising operatively linking the nucleic acid to an agent that enhances cell internalization or up-take, or a cell targeting agent.

216. The method of claim 215, wherein the cell internalization or up-take enhancing agent is selected from transferrin, asialoglycoprotein or streptavidin.

217. The method of claim 215, wherein the cell targeting agent comprises a vector.

218. The method of claim 217, wherein the vector to which the agent is operatively linked comprises a prokaryotic or eukaryotic vector.

219. The method of claim 173, wherein the nucleic acid comprises an oligo of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, or SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO: 7 to SEQ ID NO: 966, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

220. The method of claim 191, wherein the surfactant is selected from polyoxy

ethylene 23 lauryl ether (Brij 35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC®), tyloxapol (Exosurf®), phospholipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}C_{10}$ (Atovaquone®).

221. The method of claim 173, wherein the hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, or lung allergy(ies) or inflammation, is associated with asthma or a disease or condition associated with asthma.

222. A diagnostic or therapeutic device adapted for delivering a respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation of particle size about 0.5 μ to about 500 μ, the formulation comprising a nucleic acid which comprises at least one oligonucleotide (oligo) effective for diagnosing or treating hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, asthma, or lung allergy(ies) or inflammation, or a disease or condition associated with either of them, the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, or increased levels of, adenosine bronchoconstriction, asthma, or lung allergy(ies) or inflammation, or being anti-sense to the corresponding mRNA; the nucleic acid comprising one or more oligo(s), their mixtures, or their pharmaceutically or veterinarily acceptable salts.

223. The device of claim 222, comprising a nebulizer adapted for delivering single metered doses of the formulation as a solid powdered or liquid aerosol or spray of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ.

224. The device of claim 222, which comprises an insufflator adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and for producing a solid powdered or liquid aerosol or spray of particle size about 0.5μ to about 10 μ or about 10 μ to about 500 μ, and wherein the formulation is provided separately in a piercable or openable capsule(s) or cartridge(s) as a nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ.

225. The device of claim 222, which comprises a pressurized inhaler that delivers a solid powdered or liquid aerosol or spray formulation of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ; and wherein the formulation comprises a suspension, solution, emulsion or dry powdered aerosol or spray formulation of the nucleic acid of particle size about 0.05 μ to about 50 μ or about 10 μ to about 500 μ.

226. The pressurized inhaler of claim 225 further comprising, in separate containers, a propellant and pressurized means for delivery adapted for delivering a solid p wdered or liquid

aerosol or spray, and instructions for loading into the delivery device the inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation, and joining the device with the propellant and the pressurized delivery means.

227. The pressurized inhaler of claim 225, further comprising a propellant and propellant delivery means, wherein the pressurized inhaler delivers the formulation as a liquid or solid powdered aerosol or spray.

228. The device of claim 222, which is adapted for receiving and piercing or opening a capsule(s) or cartridge(s), and wherein the formulation is provided separately in a capsule(s) or cartridge(s).

229. The kit of claim 164, wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' region of a gene encoding a polypeptide selected from an adenosine A_1 receptor, adenosine A_{2a} receptor, adenosine A_{2b} receptor, or adenosine A_3 receptor.

230. The kit of claim 229, for diagnosis or treatment of sepsis, pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome (RDS), acute respiratory distress syndrome (ARDS), pain, cystic fibrosis (CF), pulmonary hypertension, pulmonary vasoconstriction, emphysema or chronic obstructive pulmonary disease (COPD).

231. The kit of claim 164, wherein the nucleic acid comprises an oligo of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 996, or SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO: 7 to SEQ ID NO: 996, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA Sulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

232. The composition of claim 108, which comprises particle sizes of about 0.5μ to about 10 μ or about 10 μ to about 500 μ.

233. The nucleic acid of claim 108, which is operatively linked to a vector.

234. A single cell, comprising the nucleic acid of claim 233.

S:\legal\00672\Claims 01-8-21 (clean)

genes, RNA and flanking regions that are devoid, or have a low T/U content, or alternatively one or more of the adenosine(s) present in the anti-sense oligonucleotide(s) are substituted with other nucleotide bases, so called universal bases, which bind to thymidine (T) but lack the ability to activate adenosine receptors and otherwise may not activate adenosine receptors. Given that adenosine (A) is a nucleotide base complementary to thymidine (T) and uridine (U), when a T appears in the DNA or a U in the RNA target, the anti-sense oligo will have an A at the same position.

The method of the present invention may be used to treat ailments associated with or causing bronchoconstriction, allegy(ies) and/or inflammation associated with any of the diseases and conditions described above in a subject, regardless of its cause. The anti-sense agent(s) of the invention have preferably a low (or reduced) A content to prevent its liberation upon in vivo degradation of the agent(s), preferably up to about 15%, more preferably up to about 10%, still more preferably up to about 5%, and even more preferred being devoid of A ("desadenosine oligos").

The oligos of this invention may be obtained by first selecting fragments of a target nucleic acid having at least 4 contiguous nucleic acids selected from the group consisting of G and C, and then obtaining a first oligonucleotide 4 to 60 nucleotides long which comprises the selected fragment and has a T and U nucleic acid content of up to and including about 15%. The latter step may be conducted by obtaining a second oligonucleotide 4 to 60 nucleotide long comprising a sequence which is anti-sense to the selected fragment, the second oligonucleotide having an adenosine base content of up to and including about 15%. This method may also comprise, when the selected fragment comprises at least one thymidine base, substituting an adenosine base in the corresponding nucleotide of the anti-sense fragment with a universal base selected from the group consisting of heteroaromatic bases which bind to a thymidine base but have antagonist activity and less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} and A_3 receptors, and heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a}